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(FILE 'HOME' ENTERED AT 17:46:18 ON 14 FEB 2001)

FILE 'MEDLINE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 17:46:38 ON 14 FEB 2001

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L1          568 S CD39
L2       245346 S PLATELET(3A)AGGREGATION OR STROKE OR ADPASE
L3           99 S L1 AND L2
L4         6577 S INTRACEREBRAL(6A)HEMORRHAGE
L5            0 S L3 AND L4
L6         1934 S L4 AND L2
L7       443683 S THROMBOTIC OR ISCHEMI?
L8          938 S L6 AND L7
L9        38403 S INHIBIT?(5A)(PLATELET(3A)AGGREGATION OR STROKE OR
LEUKOCYTE(3
L10          22 S L8 AND L9
L11           4 S INCREAS?(5A)(ADP(5A)CATABOLISM)
L12           0 S L8 AND L11
L13          17 DUP REM L10 (5 DUPLICATES REMOVED)
```

=> d au ti so 1-17 ab l13

L13 ANSWER 1 OF 17 MEDLINE

AU Carlsson J; Miketic S; Batge R; Riedel P; Rahlf G; Tebbe U

TI [Ticlopidine-associated **thrombotic** thrombocytopenic purpura (Morbus Moschcowitz)].
Ticlopidin-assoziierte thrombotisch-thrombozytopenische Purpura (Morbus Moschcowitz).

SO MEDIZINISCHE KLINIK, (2000 Jan 15) 95 (1) 44-8.
Journal code: M9K. ISSN: 0723-5003.

AB ANAMNESIS AND CLINICAL FINDINGS: A 75-year-old woman with a history of recurrent **ischemic** cerebral events was admitted with acute unspecific neurological symptoms and fever. EXAMINATION: **Intracerebral hemorrhage** due to hypertension and antithrombotic therapy with ticlopidine was ruled out with cranial computed tomography. Laboratory findings on admission included thrombocytopenia (12/nl), renal insufficiency (serum creatinine 1.6 mg/dl) and LDH elevation (1,218 U/l). The hemoglobin on admission was normal. THERAPY AND CLINICAL COURSE: In the presence of rapidly declining hemoglobin values and fragmentation of red cells **thrombotic** -thrombocytopenic purpura (TTP) was diagnosed and the patient received fresh frozen plasma. Shortly after the plasma infusion the patient's condition deteriorated rapidly showing clinical signs of an allergic shock. In the sequel of 24 to 48 hours the patient developed renal failure, severe anemia and the thrombocyte count fell to 5/nl. The patient was mechanically ventilated during the next 48 hours and needed intravenous catecholamines. Even after restoration of spontaneous respiration and cessation of pharmacological sedation the patient remained comatose. Cranial computed tomography on the fourth day after admission showed multiple infarction syndrome. The patient died on the ninth day after admission in status epilepticus which could not be stopped with pharmacological means. CONCLUSIONS: The combination of neurological

symptoms, thrombocytopenia, fever, renal failure and hemolytic anemia in a patient taking ti[redacted]pidine points to a diagnosis o[redacted]TP. The high mortality of TTP can probably only be reduced by ea[redacted]y plasmapheresis.

L13 ANSWER 2 OF 17 MEDLINE
AU Wong K S
TI Risk factors for early death in acute **ischemic stroke** and **intracerebral hemorrhage**: A prospective hospital-based study in Asia. Asian Acute **Stroke** Advisory Panel.
SO STROKE, (1999 Nov) 30 (11) 2326-30.
Journal code: V2J. ISSN: 0039-2499.
AB BACKGROUND AND PURPOSE: In Asia, there has been no international study to investigate the risk factors for early death in patients with **ischemic stroke** and **intracerebral hemorrhage**. METHODS: We conducted a prospective study of consecutive patients with acute **stroke** who were admitted to 36 participating hospitals in China, India, Indonesia, Korea, Malaysia, the Philippines, Singapore, Taiwan, Thailand, and Vietnam. With the use of a simple identical data sheet, we recorded the demographics and cardiovascular risk factors of each patient. Early death was defined as death on discharge from the acute hospital. RESULTS: We enrolled 2403 patients with **ischemic stroke** and 783 patients with **intracerebral hemorrhage**. Among patients with **ischemic stroke**, previous use of antiplatelet drugs (adjusted odds ratio [OR] 0.53; 95% confidence interval [CI] 0. 30 to 0.95) and relatively young age group 56 to 75 years (OR 0.65; 95% CI 0.42 to 1.00) were protective factors; atrial fibrillation (OR 2.23; 95% CI 1.40 to 3.57), **ischemic** heart disease (OR 2.03; 95% CI 1.37 to 3.05), diabetes (OR 1.52; 95% CI 1.04 to 2.22), and ex-smoker status (OR 2.18; 95% CI 1.18 to 4.05) were risk factors for early death. Among patients with **intracerebral hemorrhage**, hypertension (OR 0.56; 95% CI 0.38 to 0.82) and young age group 56 to 75 years old (OR 0.55; 95% CI 0.34 to 0.87) were associated with lower death rate, whereas diabetes (OR 1.74; 95% CI 1.01 to 2.98) was a risk factor for early death.
CONCLUSIONS: In Asian patients with **stroke**, previous use of antiplatelet drugs nearly halved the risk of early death in patients with **ischemic stroke**, whereas atrial fibrillation, **ischemic** heart disease, diabetes, and ex-smoker status were risk factors for early death. Among patients with **intracerebral hemorrhage**, diabetes was associated with early death, whereas young age group and hypertension were associated with lower death rates, though no clear explanation for the hypertension association could be discerned from the data available.

L13 ANSWER 3 OF 17 MEDLINE
AU del Zoppo G J
TI Antithrombotic treatments in acute **ischemic stroke**.
SO THROMBOSIS AND HAEMOSTASIS, (1999 Aug) 82 (2) 938-46. Ref: 54
Journal code: VQ7. ISSN: 0340-6245.
AB A therapeutic role for antiplatelet agents and anticoagulants within 6 hours of the onset of **ischemic stroke** symptoms has not been tested. With one exception, their use in early **stroke** (< 48 hours) did not produce a favorable outcome. The use of rt-PA in appropriate patients presenting with **ischemic stroke** within 3 hours of symptom onset has been accompanied by significant benefit, which has exceeded the risk of **intracerebral hemorrhage** in one trial. The recent group of clinical studies has provided evidence for factors which may contribute to hemorrhagic transformation. These studies also demonstrate the following: i) recanalization of carotid and vertebrobasilar artery territory occlusions is technically feasible within 3 to 6 hours of symptom onset, ii) the frequency of hemorrhage is increased in **ischemic stroke** patients receiving PAs, iii) the interval from symptom onset to treatment

to achieve clinical improvement varies individually and contributes to hemorrhagic risk, and iv) the optimal PAs, their dose-rate, and delivery systems have not been defined in either the carotid or vertebrobasilar territory. Taken together, the NINDS trial, ECASS, and ECASS II indicate the enormous importance of patient selection to reduce the hemorrhagic risk which accompanies the use of PAs in **stroke**. However, it is currently not possible to separate benefit from hemorrhagic risk in a given patient based upon simple clinical criteria, although contributors to this risk have been identified. Clearly, attempts to reduce the risk of hemorrhage should contribute to the overall benefit of selected **ischemic stroke** patients treated with rt-PA and with other PAs. This experience may also provide a clinical basis for the prospective study of antiplatelet agents and anticoagulants in acute **ischemic stroke**.

L13 ANSWER 4 OF 17 MEDLINE
AU Franco C M; Fukujima M M; de Oliveira R de M; Gabbai A A
TI Moyamoya disease. Report of three cases in Brazilian patients.
SO ARQUIVOS DE NEURO-PSIQUIATRIA, (1999 Jun) 57 (2B) 371-6.
Journal code: 8WY. ISSN: 0004-282X.
AB Moyamoya disease (MMD) is a chronic occlusive cerebrovascular disease of unknown etiology reported mainly in the Japanese. Most cases occur in children. The disease is rare in non-Oriental adults manifesting itself mostly as **intracerebral hemorrhages**. We describe MMD in 2 non-Oriental young adults and one adolescent that developed cerebral infarctions. The adults were medicated with aspirin and no medication was given to the adolescent. All patients did not deteriorate in a follow-up period from 1 to 4 years. Although rare, MMD is an important cause of **stroke** in young individuals and may well be underreported: only 18 patients have been reported till 1997 in Brazil. Neurologists should include MMD in differential diagnosis of **ischemic** and hemorrhagic **strokes** in young adults.

L13 ANSWER 5 OF 17 MEDLINE
AU Fisher M
TI Antithrombotic and thrombolytic therapy for **ischemic stroke**.
SO J Thromb Thrombolysis, (1999 Apr) 7 (2) 165-9. Ref: 24
Journal code: DDY. ISSN: 0929-5305.
AB Anthithrombotic therapy is widely used as primary and secondary preventative treatment for **ischemic** cerebrovascular disease. Aspirin modestly reduces the risk for subsequent **ischemic stroke** after a transient **ischemic** attack or initial **stroke**. Adding dipyridamole may enhance this benefit. Ticlopidine confers a small additional benefit, but with more side effects and cost. The best dose of aspirin remains unsettled, but recent studies support the concept of very early initiation of treatment. Intravenous and subcutaneous heparin or low-molecular-weight heparin is not recommended because of enhanced bleeding side effects, unless venous thrombosis in debilitated patients is a concern. Thrombolytic therapy with rt-PA was recently demonstrated to improve outcome in **ischemic stroke** patients treated within 3 hours of onset. However, the risk-benefit ratio is narrow because of the substantial risk for **intracerebral hemorrhage** with rt-PA. An enhanced ability to identify patients at risk for bleeding and newer thrombolytic drugs may expand the utility of this therapy, as would extending the time window beyond the current 3-hour period. Clinicians should anticipate continued advances in the fields of antithrombotic and thrombolytic therapy for **ischemic stroke** over the next few years.

L13 ANSWER 6 OF 17 MEDLINE DUPLICATE 1

AU Choudhri T F; Hoh B L; Prestigiacomo C J; Huang J; Kim L J; Schmidt A M; Kisiel W; Connolly E S Jr; Pinsky D J

TI Targeted inhibition of intrinsic coagulation limit erebral injury in **stroke** without increasing **intracerebral hemorrhage**.

SO JOURNAL OF EXPERIMENTAL MEDICINE, (1999 Jul 5) 190 (1) 91-9.
Journal code: I2V. ISSN: 0022-1007.

AB Agents that restore vascular patency in **stroke** also increase the risk of **intracerebral hemorrhage** (ICH). As Factor IXa is a key intermediary in the intrinsic pathway of coagulation, targeted inhibition of Factor IXa-dependent coagulation might **inhibit** microvascular thrombosis in **stroke** without impairing extrinsic hemostatic mechanisms that limit ICH. A competitive inhibitor of native Factor IXa for assembly into the intrinsic Factor X activation complex, Factor IXai, was prepared by covalent modification of the Factor IXa active site. In a modified cephalin clotting time assay, in vivo administration of Factor IXai caused a dose-dependent increase in time to clot formation (3.6-fold increase at the 300 micrograms/kg dose compared with vehicle-treated control animals, $P < 0.05$). Mice given Factor IXai and subjected to middle cerebral artery occlusion and reperfusion demonstrated reduced microvascular fibrin accumulation by immunoblotting and immunostaining, reduced 111In-labeled platelet deposition (42% decrease, $P < 0.05$), increased cerebral perfusion (2.6-fold increase in ipsilateral blood flow by laser doppler, $P < 0.05$), and smaller cerebral infarcts than vehicle-treated controls (70% reduction, $P < 0.05$) based on triphenyl tetrazolium chloride staining of serial cerebral sections. At therapeutically effective doses, Factor IXai was not associated with increased ICH, as opposed to tissue plasminogen activator (tPA) or heparin, both of which significantly increased ICH. Factor IXai was cerebroprotective even when given after the onset of **stroke**, indicating that microvascular thrombosis continues to evolve (and may be inhibited) even after primary occlusion of a major cerebrovascular tributary.

L13 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2001 ACS

IN Pinsky, David J.; Stern, David; Schmidt, Ann Marie; Rose, Eric A.; Connoly, E. Sander; Solomon, Robert A.; Prestigiacomo, Charles J.

TI Methods using selectin antagonists, carbon monoxide, and inactivated factor IX for treating an **ischemic** disorder and improving **stroke** outcome

SO PCT Int. Appl., 230 pp.
CODEN: PIXXD2

AB A method for treating an **ischemic** disorder in a subject comprises administering to the subject a pharmaceutically acceptable form of a selectin antagonist in a sufficient amt. over a sufficient time to prevent white blood cell accumulation. Also provided is a method for treating an **ischemic** disorder in a subject which comprises administering to the subject carbon monoxide gas in a sufficient amt. over a sufficient time. Further provided is a method for treating an **ischemic** disorder in a subject which comprises administering to the subject a pharmaceutically acceptable form of inactivated Factor IX in a sufficient amt. over a sufficient time to inhibit coagulation.

L13 ANSWER 8 OF 17 SCISEARCH COPYRIGHT 2001 ISI (R)

AU Jean W C; Spellman S R; Nussbaum E S; Low W C (Reprint)

TI Reperfusion injury after focal cerebral **ischemia**: The role of inflammation and the therapeutic horizon

SO NEUROSURGERY, (DEC 1998) Vol. 43, No. 6, pp. 1382-1396.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0148-396X.

AB RECENT EVIDENCE INDICATES that thrombolysis may be an effective therapy

for the treatment of acute **ischemic stroke**. However, the reperfusion of **ischemic** brain comes with a price. In clinical trials, patients treated with thrombolytic therapy have shown a 6% rate of **intracerebral hemorrhage**, which was balanced against a 30% improvement in functional outcome over controls. Destruction of the microvasculature and extension of the infarct area occur after cerebral reperfusion. We have reviewed the existing data indicating that an inflammatory response occurring after the reestablishment of circulation has a causative role in this reperfusion injury. The recruitment of neutrophils to the area of **ischemia**, the first step to inflammation, involves the coordinated appearance of multiple proteins. Intercellular adhesion molecule-1 and integrins are adhesion molecules that are up-regulated in endothelial cells and leukocytes. Tumor necrosis factor-alpha, interleukin-1, and platelet-activating factor also participate in leukocyte accumulation and subsequent activation. Therapies that interfere with the functions of these factors have shown promise in reducing reperfusion injury and infarct extension in the experimental setting. They may prove to be useful adjuncts to thrombolytic therapy in the treatment of acute **ischemic stroke**.

L13 ANSWER 9 OF 17 MEDLINE DUPLICATE 2

AU Choudhri T F; Hoh B L; Zerwes H G; Prestigiacomo C J; Kim S C; Connolly E S Jr; Kottirsch G; Pinsky D J

TI Reduced microvascular thrombosis and improved outcome in acute murine **stroke** by **inhibiting** GP IIb/IIIa receptor-mediated **platelet aggregation**.

SO JOURNAL OF CLINICAL INVESTIGATION, (1998 Oct 1) 102 (7) 1301-10. Journal code: HS7. ISSN: 0021-9738.

AB Treatment options in acute **stroke** are limited by a dearth of safe and effective regimens for recanalization of an occluded cerebrovascular tributary, as well as by the fact that patients present only after the occlusive event is established. We hypothesized that even if the site of major arterial occlusion is recanalized after **stroke**, microvascular thrombosis continues to occur at distal sites, reducing postischemic flow and contributing to ongoing neuronal death. To test this hypothesis, and to show that microvascular thrombosis occurs as an ongoing, dynamic process after the onset of **stroke**, we tested the effects of a potent antiplatelet agent given both before and after the onset of middle cerebral arterial (MCA) occlusion in a murine model of **stroke**. After 45 min of MCA occlusion and 23 h of reperfusion, fibrin accumulates in the ipsilateral cerebral hemisphere, based upon immunoblotting, and localizes to microvascular lumena, based upon immunostaining. In concordance with these data, there is a nearly threefold increase in the ipsilateral accumulation of 111In-labeled platelets in mice subjected to **stroke** compared with mice not subjected to **stroke**. When a novel **inhibitor** of the glycoprotein IIb/IIIa receptor (SDZ GPI 562) was administered immediately before MCA occlusion, platelet accumulation was reduced 48%, and fibrin accumulation was reduced by 47% by immunoblot densitometry. GPI 562 exhibited a dose-dependent reduction of cerebral infarct volumes measured by triphenyltetrazolium chloride staining, as well as improvement in postischemic cerebral blood flow, measured by laser doppler. GPI 562 caused a dose-dependent increase in tail vein bleeding time, but **intracerebral hemorrhage** (ICH) was not significantly increased at therapeutic doses; however, there was an increase in ICH at the highest doses tested. When given immediately after withdrawal of the MCA occluding suture, GPI 562 was shown to reduce cerebral infarct volumes by 70%. These data support the hypothesis that in **ischemic** regions of brain, microvascular thrombi continue to accumulate even after recanalization of the MCA, contributing to postischemic hypoperfusion and ongoing neuronal damage.

L13 ANSWER 10 OF 17 MEDLINE
AU Creager M A
TI Results of the CAPRIE trial: efficacy and safety of clopidogrel. Clopidogrel versus aspirin in patients at risk of ischaemic events.
SO VASCULAR MEDICINE, (1998) 3 (3) 257-60. Ref: 8
Journal code: C19. ISSN: 1358-863X.
AB The recent CAPRIE trial (clopidogrel versus aspirin in patients at risk of ischaemic events) compared clopidogrel with aspirin in reducing the risk of vascular events in 19,185 patients with clinical manifestations of atherosclerosis. Participants were randomized to receive daily oral clopidogrel (75 mg) or aspirin (325 mg). Treatment periods ranged from 1 to 3 years. The primary outcome measurement was an aggregate of myocardial infarction, **ischemic stroke** and vascular death. Event rates of 5.32% and 5.83% were associated with clopidogrel and aspirin therapy, respectively. Clopidogrel therapy resulted in a relative risk reduction of 8.7% (CI 0.3-16.5%) compared with aspirin therapy ($p = 0.043$). Gastrointestinal hemorrhages occurred in 1.99% of patients treated with clopidogrel and 2.66% of patients treated with aspirin ($p < 0.002$). There were no significant treatment-based differences in the rates of **intracerebral hemorrhages** and hemorrhagic deaths or thrombocytopenia. These results indicate that clopidogrel is more effective and safer than aspirin in reducing adverse cardiovascular events in patients with atherosclerosis.

L13 ANSWER 11 OF 17 MEDLINE
AU Buttner T; Hellwig K; Muller T; Kuhn W
TI Intravenously administered acetylsalicylic acid in combination with low-dose heparin in acute **ischemic stroke**: a safety analysis.
SO CLINICAL NEUROPHARMACOLOGY, (1998 Jan-Feb) 21 (1) 48-51.
Journal code: CNK. ISSN: 0362-5664.
AB Although therapy with acetylsalicylic acid (aspirin, ASA) is well established in secondary prevention of **stroke**, efficacy and side effects of this substance in acute **stroke** treatment are undetermined. ASA may be useful in acute cerebral **ischemia** because of its potential to prevent thrombus propagation and neuronal damage. A total of 268 patients with an acute cerebral **ischemia**, who were admitted to our **stroke** unit within 24 hours after **stroke**, were treated with intravenously administered ASA (0.5 g/day) in combination with low-dose heparin. The functional status of the patients was assessed after 1 month using the modified Rankin Scale. Eighteen (6.7%) patients died during the observation period. The functional status according to Rankin Scale was classified as stage 0 in 76 (28.3%), 1 in 59 (22.0%), 2 in 39 (14.6%), 3 in 32 (12.3%), 4 in 36 (13.4%), and 5 in 7 (2.6%) patients. A symptomatic secondary **intracerebral hemorrhage** was seen in one patient. Gastrointestinal symptoms were observed in 13 (4.8%) patients, including five instances of gastrointestinal bleeding. Further complications were allergic reactions to aspirin (one) and hematuria (one). Recurrent cerebral **ischemia** occurred in nine (3.3%) patients (five with transient **ischemic** attack or minor **stroke**) during the observation period. We conclude that treatment of acute **ischemic stroke** with intravenously applied aspirin in combination with low-dose heparin is safe. Efficacy of this therapy should be elucidated in a controlled trial.

L13 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2001 ACS
AU Del Zoppo, Gregory J.
TI The role of platelets in **ischemic stroke**

SO Neurology (1998), 51(3, Suppl. 3, Current Advances in the Management of Stroke), S9-S14
CODEN: NEURAI; ISSN: 0028-3878

AB A review, with 32 refs. Platelets have assumed a role in the development of focal cerebral **ischemia** by virtue of their participation in thromboemboli that may initiate **stroke** symptoms. Platelets are one component of the blood-vascular axis responsible for preventing hemorrhage. Activated platelets initiate hemostatic plug formation and provide a scaffolding for coagulation activation. Platelets are activated by a no. of stimuli, such as exposure of the vascular subendothelium, fibrin deposition, and abnormal surfaces, e.g., atheromata. A no. of observations, including the appearance of platelet thrombi on atheromata in situ, indicate that platelet physiol. is relevant to **stroke**. In addn., certain antiplatelet agents (e.g., aspirin) significantly reduce the incidence of **ischemic stroke** after initial transient **ischemic** attacks. Aspirin, the combination of aspirin and dipyridamole, and ticlopidine have all been shown to be useful in reducing the frequency of secondary **stroke** events. Clopidogrel has been shown to reduce the frequency of secondary vascular **ischemic** events when **stroke**, myocardial infarction, and peripheral arterial disease are considered together. Unfortunately, all antithrombotic agents carry a potential risk for inducing symptomatic **intracerebral hemorrhage** during **ischemic stroke**. The mechanism by which this may happen with antiplatelet agents has not yet been detd. As in other areas of **stroke** treatment, it is the balance between efficacy in redn. of symptomatic **thrombotic** events and the risk for hemorrhage that will define benefit.

L13 ANSWER 13 OF 17 MEDLINE
AU Alvarez-Sabin J; Calvo G; Morros R
TI [Secondary prevention of **ischemic strokes**: effect of dosage of aspirin].
Prevencion secundaria del ictus isquemico. Efecto de la dosis en el perfil de la aspirina.
SO REVISTA DE NEUROLOGIA, (1997 Apr) 25 (140) 541-4.
Journal code: CG9. ISSN: 0210-0010.

AB INTRODUCTION AND OBJECTIVE: The value of acetylsalicylic acid (ASS) in the secondary prevention of **ischemic stroke** is well established. However, the optimum dose of AAS for **stroke** -threatened patients remains unsettled. This paper reviews the pattern of adverse reactions to AAS and their relationship to the dosage of ASS evaluated. METHOD: All the clinical trials in which AAS was used as the sole antiaggregant in the secondary prevention of **ischemic stroke** were reviewed. The crude odds ratio for the different adverse reactions was calculated using three sub tests: AAS versus placebo; AAS < 330 mg/d versus AAS > 330 mg/d; and each dosage level versus a placebo. RESULTS: There is an increased risk associated with the use of AAS as compared to a placebo with respect to gastrointestinal bleeding (OR 2.3, IC 95% (1.6-4.1)), peptic ulcer (10.1 (2.5-85.2)), **intracerebral hemorrhage** (2.2 (1.3-4)) and other hemorrhagic phenomena (2.6 (2-3.3)). CONCLUSIONS: There seems to be a direct relationship between the dosage of AAS and the frequency with which adverse reactions occur, except in the case of **intracerebral hemorrhage**. In the latter case there was no relationship with the dose given (0.8 (0.5-1.4)).

L13 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2001 ACS
AU Laux, V.; Elger, B.; Schwarz, M.; Hornberger, W.
TI Fibrinogen lowering with ancrod (Arvin) in acute **ischemic**

stroke: preclinical data confirm the efficient and safe rheological principle
SO World Congr. Microcirc., 6th (1996), 297-300. Edi (s): Messmer, Konrad;
Kuebler, Wolfgang M. Publisher: Monduzzi Editore, Bologna, Italy.
CODEN: 64KQAW
AB Ancrod (Arvin), a purified fraction of the venom from the Malayan pit viper Agkistrodon rhodostoma, produces rapid and effective defibrinogenation. This results in lowering of blood viscosity and in inhibition of thrombus formation. These effects together with a panel of secondary mechanisms such as redn. of erythrocyte **aggregation**, **inhibition** of **platelet** adhesion and enhancement of endogenous fibrinolysis may form the basis of beneficial results obtained with ancrod in cerebrovascular disorders. Ancrod is able to ameliorate **ischemic** edema in an exptl.-induced **stroke** model in rats. Moreover, in a model of **intracerebral hemorrhage**, ancrod reduces the extent of bleeding. Thus, ancrod represents an efficient and safe concept in improvement of microcirculation during acute **ischemic** brain infarction even in low flow states.

L13 ANSWER 15 OF 17 MEDLINE
AU Delcker A; Diener H C
TI [Neurological diagnosis and therapeutic measures in cerebral embolism]. Neurologische Diagnostik und therapeutische Massnahmen bei zerebralen Embolien.
SO HERZ, (1991 Dec) 16 (6) 434-43. Ref: 83
Journal code: F88. ISSN: 0340-9937.
AB **Stroke** is caused by **intracerebral** or subarachnoid **hemorrhage** in about 15% of clinical presentations and the remaining 85% result from **ischemia**. About 15% of **ischemic strokes** are caused by emboli arising from the heart. In younger patients (18 to 50 years) with **ischemic strokes** or transient **ischemic** attacks (TIA), the incidence of cardiac embolism is increased to 23 to 36%. Diagnosis: a) Symptoms: Individual neurologic symptoms of **stroke** do not provide sensitive or specific indications of the underlying mechanism. In 25 to 82% of patients with possible embolic **stroke**, there is an acute onset with initially maximal manifestation of neurologic deficits as well an initial loss of consciousness in 20%. Antecedent TIAs occur in 11 to 30% but are more frequently associated with arteriosclerotic vascular disease. **Stroke** due to cardiac embolism mostly involves the cortex of both hemispheres and causes its symptoms through occlusion of isolated arterial branches. Cerebral infarctions with isolated Wernicke aphasia, global aphasia without hemiparesis and isolated syndromes of the posterior cerebral artery are frequently due to cardiac embolism. The **strokes** in 16 to 22% of those caused by cardiac embolism are found in subcortical regions. Amaurosis fugax is most frequently due to high-grade stenosis of the internal carotid artery. In association with cardiac embolism, secondary hemorrhage into the infarcted zone can frequently be seen on CT scans. b) Diagnostic procedures: In the case of cardiac embolism, the computer tomography (CT) usually shows infarction in or near the cortex in the region of the middle or posterior cerebral artery. About 10 to 20% of **strokes** due to cardiac embolism show secondary hemorrhage after the event, more frequently in association with large infarcts and in patients on anticoagulant treatment. Angiography can provide indirect evidence of embolic origin by showing occlusion of an intracerebral artery in the absence of arteriosclerotic changes. Traditional echocardiography may detect a possible source of embolism in 10% of all patients with **ischemic stroke**, only in 1.5%, however, in patients with no clinical signs of heart disease. Transesophageal echocardiography has a higher sensitivity for detection of

sources of cardiac embolism. The use of magnetic resonance tomography and ultrafast CT will assume greater importance in the future. Holter monitoring of the ECG in patients with acute **ischemic stroke** or TIAs detects arrhythmias possibly responsible for emboli in about 2%. High-risk patients: The most common cause of cardiac embolism is atrial fibrillation (45%), followed by **ischemic** heart disease (15%) and in 10% each, aneurysm, rheumatic heart disease, prosthetic valve replacement and other cardiac diseases.(ABSTRACT TRUNCATED AT 400 WORDS)

L13 ANSWER 16 OF 17 MEDLINE
AU Feinberg W
TI Antithrombotic therapy in **stroke** and transient **ischemic** attacks.
SO AMERICAN FAMILY PHYSICIAN, (1989 Nov) 40 (5 Suppl) 53S-59S. Ref: 34
Journal code: 3BT. ISSN: 0002-838X.
AB Approximately 85 percent of **strokes** are caused by infarction, with the remainder due to subarachnoid or **intracerebral hemorrhage**. Eighty percent of **ischemic strokes** are attributed to cerebrovascular disease, 15 percent to cardiogenic embolism and 5 percent to more unusual causes. Risk factors for **stroke** include hypertension and lifestyle choices. Recommendations for anticoagulant prophylaxis, treatment and dosage are provided.

L13 ANSWER 17 OF 17 MEDLINE
AU Flugel K A
TI [Prevention and therapy of **stroke**].
Prophylaxe und Therapie des Schlaganfalls.
SO FORTSCHRITTE DER MEDIZIN, (1980 May 29) 98 (20) 773-8.
Journal code: F62. ISSN: 0015-8178.
AB The effectiveness of preventive and therapeutic measures depends upon their adequacy in the individual diagnostic situation. This is also true for **stroke** which is a superimposed concept for different mechanisms leading to acute localized brain **ischemia**. For the choice of treatment we have to consider in each case the actual clinical situation, i.e. the natural stage of disease, the localization of cerebral dysfunction and its etiology and pathogenesis. Thus transient **ischemic** attacks (TIA), completed **stroke** with prolonged complete, partial or no recovery and progressive **stroke** (**stroke** in evolution) demand different treatment. Concerning pathogenesis it is important to differentiate between **intracerebral hemorrhage, ischemia** due to extracranial carotid stenosis or occlusion, intracranial arterial thrombosis, predominantly hemodynamic pathogenesis and embolism of cardiac origin. Prevention of **stroke** may be of general kind like treatment of hypertension or other risk factors for apoplexy, and there are more specific measures like surgery of vascular obliteration and treatment with agents **inhibiting platelet aggregation** (Aspirin) or anticoagulants. The indications for the various surgical and medical procedures are discussed. Because of the risk of hemorrhagic complications the indication for anticoagulants is limited considerably. The treatment of completed **stroke** has to consider the normalization of basic functions (cardiocirculatory, respiration, water-electrolyte balance a.o.). Vasoactive and especially vasodilatatory drugs are not recommended in the acute stage of **stroke**, as their effectiveness is not secure and may even be disadvantageous. **Ischemic** brain edema is treated with mannitol or sorbit and with dexamethasone although its effectiveness has not yet been proven. Low molecular dextran solution is supposed to improve microcirculation in the **ischemic** tissue by means of hemodilution i.e. improvement of rheological properties.

L3 ANSWER 2 OF 6 MEDLINE
AB Addition of exogenous plasminogen activator inhibitor-1 (PAI-1) to **fibrin** clots inhibits fibrinolysis in vivo. However, it is unknown whether the localized concentrations of active PAI-1 necessary to produce this antifibrinolytic effect can be recruited to acute arterial thrombi by endogenous mechanisms. We measured PAI-1 activity and antigen in porcine coronary artery thrombi that formed in response to acute vascular injury. Mean PAI-1 activity in thrombi (n = 5) was 36 +/- 5.1 micrograms/mL, which is > 2000 times its concentration in normal porcine plasma. The presence of markedly elevated concentrations of active PAI-1 in thrombi was confirmed by an immunoactivity assay and by demonstrating formation of sodium dodecyl sulfate-stable complexes after addition of 125I-urokinase to thrombus extracts. Comparative analysis of PAI-1 antigen by Western blotting and urokinase inhibition assay suggested that approximately one third of thrombus-associated PAI-1 was active. Histological examination of coronary thrombi revealed that they consisted predominantly of dense aggregates of **platelets** with interspersed islands of **fibrin**, which closely resemble the histological appearance of thrombi in patients with myocardial infarction and unstable angina pectoris. Washed porcine **platelets** prepared from peripheral blood contained sufficient PAI-1 antigen and activity to account for the concentrations observed in coronary artery thrombi. However, the specific activity of human **platelet** PAI-1 was lower than that of porcine **platelet** PAI-1 (2% versus 50% active, respectively), and human **platelets** inhibited in vitro fibrinolysis to a lesser extent than did porcine **platelets**. These results indicate that active PAI-1 accumulates in porcine coronary artery thrombi in concentrations markedly higher than those present in plasma and that PAI-1 may be an important determinant of the known resistance of **platelet**-rich thrombi to lysis by tissue-type plasminogen activator. These studies also underscore the importance of considering possible species differences in protein function when comparing **animal models** of **thrombosis** to acute coronary thrombosis in humans.

=> d 2 bib

L3 ANSWER 2 OF 6 MEDLINE
AN 97010892 MEDLINE
DN 97010892
TI High concentrations of active plasminogen activator inhibitor-1 in porcine coronary artery thrombi.
AU Fay W P; Murphy J G; Owen W G
CS Department of Internal Medicine (Cardiology), University of Michigan Medical School, Ann Arbor, USA.. wfay@umich.edu
NC HL-02728 (NHLBI)
HL-47469 (NHLBI)
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